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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	**PAPER NUMBER**
1616	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/632,737	GAO ET AL.	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *7-8, 11, 17, and ,25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9,10,12-16 and 18-31* is/are rejected.

7)☒ Claim(s) *2-6,9,10,12-16 and 18-31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/11/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-31 are pending. Applicants have amended claim 21. Claim 31 is new. Claims 7-8, 11, and 17 are withdrawn from consideration as being drawn to non-elected subject matter. **Claims 1-6, 9-10, 12-16, and 18-31 are under consideration in the instant office action.** Receipt and consideration of Applicants' IDS (submitted 12/11/2003), amended claim set, and remarks/arguments submitted on November 20, 2006 is acknowledged.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-31; wherein A is pyrazolyl) and species elections of sodium metabisulfite (sulfite compound), free-radical scavenging antioxidant (additional excipient), polysorbate 80 (surfactant), polyethylene glycol (solvent), water (cosolvent), soft gelatin capsule shells (capsule shell type), and liquid (fill material form) in the reply filed on November 20, 2006 is acknowledged. The required species election of the type of gelatin capsule is withdrawn. The traversal is on the ground(s) that the Group described in the restriction mailed on September 26, 2006 excludes subject matter that Applicants regard as their invention. The Examiner agrees with Applicants. A new Group, Group VII (claims 1-22 and 25-30), drawn to a pharmaceutical dosage form wherein the selective cyclooxygenase-2 inhibitory drug of low water solubility described by formula I, wherein A is not pyrazolyl, furanyl, pyridinyl, isoxazolyl, cyclopentenoyl, or pyridazinonyl is hereby added to the groups set forth in the restriction mailed on 9/26/2006. The Examiner acknowledges the presence of a typographical error in the previous restriction requirement wherein Groups II-VI were

described as including claims 1-22 and 25-30 and "drawn to claims 1-30". The description of Groups II-VI should not have included the phrase "drawn to claims 1-30." The Examiner acknowledges that Group VI was incorrectly referred to as Group IV on page 3 of the restriction requirement mailed on 9/26/2006.

Specification

The disclosure is objected to because of the following informalities: (1) there is an apparent typographical error in [0093], wherein the text describing F1 actually is describing the results tabulated in Table 2 for F2 and (2) the number of the paragraphs is incorrect, because on page 7 after paragraph [0028] the paragraph numbering begins at [0020]. The error in the numbering of the paragraphs is propagated throughout the remainder of the specification. Appropriate correction is required.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claims 2-6, 9-10, 12-16, and 18-31 are objected to because of the following informalities: the word "claim" on line 1 of said claims is incorrectly capitalized. "Claim" is not a proper noun therefore it is grammatically incorrect to capitalize this word whenever it does not occur at the beginning of a sentence. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 9-10, 12-16, 18-20, and 25-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants' disclosure does not adequately describe all possible pharmaceutical dosage forms comprising (1) any selective cyclooxygenase-2 inhibitory drug of low water solubility and/or (2) any pharmaceutically acceptable sulfite compound. Applicants' specification does not provide adequate guidance to an ordinary skilled artisan, such that said artisan could clearly envisage the genus of compounds classified as selective cyclooxygenase-2 inhibitors (COX-2 inhibitors) of low water solubility. Compounds that inhibit cyclooxygenase-2 are a genus of compounds described solely by function and not by structure. Applicants' have not described what general chemical moieties are necessary to confer the property of cyclooxygenase-2 inhibition upon a compound. Applicants' have only adequately described a very narrow sub-genus of selective COX-2 inhibitors described by the chemical structure depicted in formula I in paragraph [0027]. The specification also lacks adequate description of all possible pharmaceutically acceptable sulfite compounds such that a person of ordinary skill in the art at the time of the instant invention could clearly envisage this genus. Applicants' disclosure does not set forth what constitutes a pharmaceutically acceptable sulfite capable of inhibiting gelatin cross-linking and/or pellicle formation. Applicants' have only provided a short list of three

possible sulfite compounds, which are considered pharmaceutically acceptable and have the required properties. Therefore, the Examiner concludes that the instant specification lacks adequate written description of all possible selective COX-2 inhibitor drugs of low water solubility as well as all possible pharmaceutically acceptable sulfite compounds.

Claims 1-6, 9-10, 12-16, 18-20, and 25-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical dosage form comprising (a) selective COX-2 inhibitor of low water solubility described by formula I in claim 21 and (b) a pharmaceutically acceptable sulfite, does not reasonably provide enablement for a pharmaceutical dosage form comprising (a) *all possible selective COX-2 inhibitors of low water solubility*. The specification does not enable any person of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. As was set forth above, Applicants' specification lacks adequate written description of the genus of low water solubility selective COX-2 inhibitors, because COX-2 inhibition is a functional description that does not enable an ordinary skilled artisan to clearly envisage what is being described. Applicants' haven't enabled an ordinary skilled artisan how to recognize a selective COX-2 inhibitor of low water solubility. That which is not adequately described cannot be enabled. Furthermore, Applicants' have not indicated what criteria are required to distinguish selective COX-2 inhibitors from non-selective COX-2 inhibitors. It is unclear if there is some threshold value for the binding constant of a potential COX-2 inhibitor that distinguishes "selective" and "non-selective" COX-2 inhibition. Therefor, because an ordinary skilled

artisan would be unable to identify low water solubility COX-2 inhibitors that are not described by formula I (e.g. celecoxib), the Examiner concludes that Applicants' have not enabled claims to pharmaceutical dosage forms comprising any possible known or yet undiscovered low water solubility COX-2 inhibitor.

Claims 1-6, 9-10, 12-16, 18-20, and 25-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical dosage form comprising (a) a selective low water solubility COX-2 inhibitor and (b) a pharmaceutically acceptable sulfite compound selected from a group consisting of sodium metabisulfite, sodium bisulfite, and sodium thiosulfate, does not reasonably provide enablement for a pharmaceutical dosage form comprising (a) a selective low water solubility COX-2 inhibitor and (b) *all possible pharmaceutically acceptable sulfite compounds*.

Aside from the three specific sulfite compounds identified in the disclosure, Applicants' have not enabled an ordinary skilled artisan to identify what constitutes a pharmaceutically acceptable sulfite compound with the ability to inhibit gelatin cross-linking and/or pellicle formation. Applicants have only provided three illustrative examples of said sulfite compounds in paragraph [0027] on page 10 of the specification. Examples do not constitute a definition and therefore do not clearly set forth the metes and bounds of the genus of pharmaceutically acceptable sulfite compounds with the property of inhibiting gelatin cross-linking and/or pellicle formation. Furthermore, as noted above, the genus of pharmaceutically acceptable sulfite compounds being able to inhibit gelatin formation and/or pellicle formation has not been adequately described.

Something that is inadequately described cannot be enabled. Therefor, because an ordinary skilled artisan would be unable to identify a pharmaceutically acceptable sulfite compound capable of inhibiting gelatin cross-linking and/or pellicle formation, excluding the group consisting of sodium metabisulfite, sodium bisulfite, and sodium thiosulfate, the Examiner concludes that Applicants' have not enabled claims to pharmaceutical dosage forms comprising any possible sulfite compound.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-6, 9-10, 12-16, and 18-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because it is unclear what is meant by the term "low water solubility." "Low water solubility" is not defined in the specification. Examples do not constitute a definition. Therefor, a person of ordinary skill in the art would not be apprised of the metes and bounds of the term "low water solubility."

Claim 5 is vague and indefinite because it refers to specific compounds in the plural. This is confusing because, there is only one compound known as alpha-tocopherol, ascorbic acid, fumaric acid, hypophosphorous acid, and malic acid, respectively. Claim 5 is further indefinite because it is unclear whether "ascrobates," "palmitates," "fumarates," and "alkyl gallates" are in reference to salts or esters of

ascorbic acid, palmitic acid, fumaric acid, and an alkyl gallic acid, respectively. Appropriate correction and/or clarification are required.

Claim 9 is vague and indefinite because it refers to specific compounds in the plural. This is confusing because, there is only one compound known as benzalkonium chloride, benzethonium chloride, cetylpyridinium chloride, dioctyl sodium sulfosuccinate, polyoxyethylene (8), propylene glycol laurate, sodium lauryl sulfate, sorbitan monolaurate, sorbitan monooleate, sorbitan monopalmitate, and sorbitan monostearate. Appropriate correction is required.

Claim 18 is vague and indefinite because it refers to a specific compound in the plural. This is confusing because, there is only one compound known as propylene glycol. Appropriate correction is required.

Claim 22 is vague and indefinite because it is unclear what constitutes pharmaceutically acceptable prodrugs of the selective COX-2 inhibitory drugs listed in said claim. Applicants' specification has not defined the term prodrugs and/or identified what are pharmaceutically acceptable prodrugs of the COX-2 inhibitor drugs listed in claim 22. Therefor, a person of ordinary skill in the art would be unable to determine the metes and bounds of what is being claimed. Appropriate correction is required.

Claim 28 is vague and indefinite because it is unclear what are the "other substances" that promote cross-linking (see line 5 of claim 28). The term "other substances" is not defined in the specification. An ordinary skilled artisan would not be apprised of the metes and bounds of what is being claimed and would be unable to ascertain its meaning from the specification. Appropriate correction is required.

Claim 29 is vague and indefinite because it is unclear what is meant by "substantially identical". The term "substantially identical" is not defined in the specification. An ordinary skilled artisan would not be apprised of the metes and bounds of what is being claimed and would be unable to ascertain the meaning of "substantially identical" from the specification. Appropriate correction is required.

Claim 29 is vague and indefinite because it is unclear what are the first and second in vitro dissolution assays to which Applicants refer. An assay is a specific experiment used to make some kind of determination. It is unclear what are the required steps and components of the two different in vitro assays. Appropriate correction is required.

Claim 29 is vague and indefinite because it is unclear what is a "reasonably short time." The instant specification does not define the term "reasonably short time" or even "short time." An ordinary skilled artisan would not be apprised of the metes and bounds of what is being claimed and would be unable to ascertain the meaning of a reasonably short time" from the specification. Appropriate correction is required.

Claim 31 recites the limitation "A is a heterocyclyl group" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 31 depends from directly from claim 22, which depends from claim 1. Neither claim 1 nor claim 22 make reference to a variable "A" or said variable being a heterocyclyl group. Appropriate correction is required.

The remaining claims are rejected for depending from a rejected claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue; and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 9-10, 12-16, 18-20, and 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Black et al. (U.S. Patent No. 5,733,909) in view of Sakuma et al. (EP 0695544).

Applicant Claims

Applicants claim a pharmaceutical dosage form comprising a fill material sealed in capsule shells wherein said fill material comprises (a) a selective COX-2 inhibitor of low water solubility and (b) at least one pharmaceutically acceptable sulfite compound, present in an amount sufficient to inhibit gelatin cross-linking and/or pellicle formation in the capsule shells upon storage.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Black teaches diphenyl stilbenes compounds of formula I as **prodrugs to COX-2 inhibitors**, which **inhibit COX-2 selectively over COX-1** and are converted in vivo to the selective inhibitors (title; abstract; col. 2, lines 45-64; col. 9, lines 15-26). Blacks' invented COX-2 inhibitors can be formulated in pharmaceutical compositions for the treatment of COX-2 mediated diseases, wherein said compositions may comprise a non-toxic therapeutically effective amount of a compound of formula I and additional active ingredients, such as another pain reliever, decongestants, antitussives, potentiators, etc. Pharmaceutical compositions suitable for oral use include **hard or soft capsules** and may comprise one or more agents selected from a group consisting of **sweetening agents, flavoring agents, coloring agents, and preserving agents** (col., 9, line 66 through col. 10, line 10). Suitable orally administrable compositions include **hard gelatin capsules or soft gelatin capsules**, wherein the active ingredient is mixed with **water** or miscible solvents such as **propylene glycol, PEGs (i.e. polyethylene glycols), ethanol**, etc. PEG is both a glycol component and a glycol ether. **Aqueous suspensions** contain the active ingredient in admixture with suitable excipients for the manufacture of suspensions, such

as **hydroxypropyl methylcellulose**, **polyoxyethylene stearate, polyoxyethylene sorbitol monooleate, polyoxyethylene sorbitan monooleate (i.e. polysorbates)**, etc. Aqueous suspensions may also comprise one or more **preservatives, coloring agents, flavoring agents, and sweetening agents** (col. 10, lines 35-56).

Sukuma teaches that hard gelatin capsules are sometimes denatured during storage under warmed conditions, which has been attributed to the presence of PEG and other compounds (e.g. triethyl citrate) are thermally decomposed to yield peroxidation products such as aldehydes and ketones which induce cross-linking (i.e. bridge formation) or polymerization in gelatin (pg. 2, lines 21-33). Sukuma has discovered that the addition of free-radical scavengers ("FRSs") in an amount of **0.01-5 % w/w**, suitable FRSs preferably include **sodium sulfite, sodium hydrogensulfite** (i.e. sodium bisulfite), **tocopherol, and ascorbic acid**, polyphosphoric acid, and pyrophosphoric acid (title; abstract; pg. 2, lines 49-50; pg. 3, lines 8-17). The FRSs may be in any form selected from powder, granules, semisolid, **solution**, and the like (pg. 3,lines 25-27). Figures 2H and 2I demonstrate that the presence of sodium sulfite and sodium hydrogensulfite (i.e. sodium bisulfite) prevented the denaturation of gelatin capsules.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Black lacks the teaching of pharmaceutical dosage forms comprising sulfite compounds. This deficiency is cured by the teachings of Sukuma.

Finding of Prima Facie Obviousness Rational and Motivation

(MPEP §2142-2143)

It would have been obvious to a person of ordinary skill in the art to combine the teachings of Black and Sukuma, because Black teaches that the pharmaceutical compositions for oral use may be in the form of hard or soft gelatin capsules. An ordinary skilled artisan would have been motivated to combine the teachings of Black and Sakuma and modify Black's invented compositions to include a sulfite compound, because the prior art has recognized the problem of the formation of cross-links in gelatin capsules as well as the ability of sulfite compounds to prevent the formation of said cross-links. A person of ordinary skill in the art would have had a reasonable expectation of success upon combination of the prior art teachings, because Sukuma's data clearly demonstrates that the presence of sulfite compounds prevents the denaturation of gelatin capsules. Black's invented selective COX-2 inhibitors would be expected to exhibit a low water solubility, because these compounds are very hydrophobic due to the stilbene moiety and the fact that substituents X and Y are typically low polarity and/or hydrophobic groups, which would not be expected to greatly enhance water solubility. Regarding the molecular weight of the PEG, and the capsule fill capacity, these are parameters that a person of ordinary skill in the art would routinely optimize to obtain the best result. The selection of a particular polysorbate (i.e. polyoxyethylene sorbitan monooleate) is well within the capability of a person of ordinary skill in the art.

In paragraph [0011] of the instant specification Applicants have stated that the observation that the presence of sulfite compounds reduces the formation of cross-links in gelatin capsules is unexpected and surprising. The Examiner respectfully disagrees because it was well known in the art (Sukuma) that sulfite compounds inhibit the

denaturation (i.e. cross-linking) of gelatin capsules. Nonetheless, even if it were surprising that sulfite compounds (i.e. sodium bisulfite and sodium sulfite) inhibit cross-linking of gelatin capsules, Applicants' data is not sufficient to overcome the instant rejection, because it is not commensurate in scope with what is being claimed. Applicants are claiming dosage forms comprising any generic selective COX-2 inhibitor of low water solubility and a sulfite compound. Applicants' have only demonstrated that soft gelatin capsules comprising a fill material comprising 4 mg/g of sodium metabisulfite, celecoxib (270 mg/g), PEG400 (335 mg/g), TWEEN 80 (195 mg/g), oleic acid (78 mg/g), HPMC (74 mg/g), propyl gallate (2 mg/g), and water (7 mg/g) demonstrate a reduction of gelatin cross-linking (see Formulation 19 results in Examples 3 and 4). Applicants' data in Example 2 has demonstrated that the presence of sodium metabisulfite, sodium bisulfite, and glycine at a concentration of 5 mg/ml in a solution comprising PEG400 and 414 microliters of formaldehyde greatly reduced the amount of formaldehyde present upon storage for three days. This data suggests that amounts of sodium metabisulfite, sodium bisulfite, and glycine of 5 mg/ml of composition might reduce gelatin cross-linking, because formaldehyde is suspected to contribute to the formation of cross-linking due to in situ capsule reactions upon storage. Nonetheless, this is insufficient to overcome the instant rejection, because it is not commensurate in scope with what is being claimed. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Claims 21-24 and 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Black et al. (U.S. Patent No. 5,733,909) in view of Sakuma et al. (EP 0695544) as applied to claims 1-6, 9-10, 12-16, 18-20, and 25-29.above, and further in view of Tanida et al. (U.S. Patent No. 6,214,378).

Applicant Claims

Applicants claim a pharmaceutical dosage form comprising a fill material sealed in capsule shells wherein said fill material comprises (a) a selective COX-2 inhibitor of low water solubility of formula I as set forth in claim 21 (e.g. celecoxib) and (b) at least one pharmaceutically acceptable sulfite compound, present in an amount sufficient to inhibit gelatin cross-linking and/or pellicle formation in the capsule shells upon storage.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Black and Sukuma have been set forth above in the instant office action. Tanida teaches capsules for oral preparations useful for treating a variety of diseases (title; abstract; claims). The active substance encapsulated by the capsules is any that could be released in the lower gastrointestinal tract, including celecoxib (col. 3, lines 12-16 and 41). When the active is an anti-inflammatory agent, it is preferred that it is a COX-2 inhibitor (col. 3, lines 56-57). Celecoxib is a COX-2 inhibitor. Tanida's formulations may include additives, such as vehicle, liquid agent, absorbefacient, etc. (col. 3, line 62 through col. 4, line 26). Liquid preparations the use of PEG 400 is exemplified. Suitable absorbefacients include **polyethylene glycol sodium dodecyl sulfate, sucrose fatty acid esters**, etc.

Ascertainment of the Difference Between Scope the Prior Art and the Claims

(MPEP §2141.012)

Black and Sukuma lack the teaching of pharmaceutical dosage forms comprising celecoxib. This deficiency is cured by the teachings of Tanida.

Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of Black/Sukuma and Tanida, because the Black/Sukuma combination teaches capsule formulations comprising a selective COX-2 inhibitor and Tanida teaches capsule formulations wherein it is preferable to utilize a COX-2 inhibitor as an anti-inflammatory agent. A person of ordinary skill in the art would have been motivated to either substitute celecoxib for Black's invented selective COX-2 inhibitors or include celecoxib as an additional active agent because Black teaches that additional active agents may be included in the composition. Furthermore, the inclusion of an additional selective COX-2 inhibitor having a different core structure would be expected to at least yield an additive effect regarding the compositions' ability to inhibit COX-2 and therefore an ordinary skilled artisan would have had a reasonable expectation of success. Regarding the possibility of substitution of celecoxib for Black's invented COX-2 inhibitors, an ordinary skilled artisan would have had a reasonable expectation of success because celecoxib is a know selective COX-2 inhibitor. As discussed supra, Applicants' data is not sufficient to overcome the instant rejection, because it does not demonstrate unexpected results, and even if it did, it would not be

sufficient, because said data is not commensurate in scope with what is being claimed. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 10, 21-23, 28-29, and 31 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 19-20, 23, and 26-31 of copending Application No. 10/633,102 (copending '102). Although the conflicting claims are not identical, they are not patentably distinct from each other because these are substantially overlapping in scope and mutually obvious. Independent claim 1 of the instant application claims a pharmaceutical dosage

form comprising a fill material sealed in capsule shells wherein said fill material comprises (a) a selective COX-2 inhibitor of low water solubility and (b) at least one pharmaceutically acceptable sulfite compound. Independent claim 19 of copending '102 claims a pharmaceutical dosage form comprising a fill material sealed in capsule shells wherein the capsule shells comprise an amine agent. Dependent claims 24-27 of copending '102 specify that the fill material comprises a drug; the drug is of low water solubility; the drug is a selective COX-2 inhibitor; and that the drug is a compound of formula (I), which is the same formula (I) depicted in claim 21 of the instant application. Although independent claim 19 does not specify that the fill material comprises a selective low water solubility COX-2 inhibitor the use of comprising language permits this component and other active agents and excipients to be present without an explicit recitation. It is also noted that independent claim 1 of the instant application utilizes comprising language too; therefor the claimed dosage forms may also comprise an amine agent in the capsule shells. For these reasons, the Examiner concludes that the cited claims of the instant application are *prima facie* obvious over the cited claims of copending '102.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-4, 10, 21-24, and 28-29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 19-20, 23, and 30-33 of copending Application No. 10/633,194 (copending '194). Although the conflicting claims are not identical, they are not patentably distinct from

each other because these are substantially overlapping in scope and mutually obvious. Independent claim 1 of the instant application has been described *supra*. Independent claim 19 of copending '194 claims a pharmaceutical dosage form comprising a fill material sealed in capsule shells, wherein the capsule shells comprise a sulfite compound and wherein the fill material comprises celecoxib. Dependent claim 23 of copending '194 specifies the total amount of sulfite compound in the capsule shell and the fill material is less than or equal to about 10% on a dry weight basis. As discussed above, the use of comprising language allows for the presence of additional unnamed excipients and active materials in the claimed dosage form. For these reasons, the Examiner concludes that the cited claims of the instant application are *prima facie* obvious over the cited claims of copending '194.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6-10 of copending Application No. 10/633,390 (copending '390). Although the conflicting claims are not identical, they are not patentably distinct from each other because these are substantially overlapping in scope and mutually obvious. Independent claim 1 of the instant application has been described *supra*. Dependent claim 6 of copending '390 claims a pharmaceutical dosage form comprising a fill material sealed in capsule shells wherein said fill material comprises (a) a selective low water solubility COX-2 inhibitor, (b) an amine agent; and (c) at least one sulfite compound. As discussed above, the use of

comprising language in both applications allows for the presence of additional unnamed excipients and/or active materials in the claimed dosage form. For these reasons, the Examiner concludes that the cited claims of the instant application are *prima facie* obvious over the cited claims of copending '390.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The Adsenuloye reference (i.e. U.S. Patent No. 5,874,106) is relevant because it teaches the inclusion of compounds to reduce cross-linking in gelatin capsules.

Claims 1-6, 9-10, 12-16, and 18-31 are rejected. Claims 2-6, 9-10, 12-16, and 18-31 are objected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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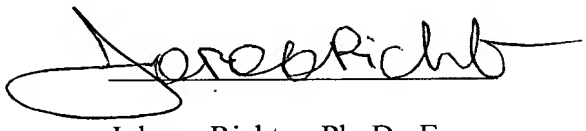

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